#### **MATTHEW HOLMES\***

# Somatic Hybridization: The Rise and Fall of a Mid-Twentieth-Century Biotechnology

#### ABSTRACT

Somatic hybridization is the particle collider of the biological world: where plant cells stripped of their cell wall are fused to create interspecific crosses containing a huge range of genetic information. This paper charts the origins of somatic hybridization and its rise and fall as a plant breeding technique. During the 1960s and 1970s, the creation of somatic hybrids through cell fusion promised a new era of crop improvement. Yet the promises of somatic hybridization were instead fulfilled by advances in recombinant DNA technology. Rather than cast somatic hybridization as a failed research program, this paper argues that a number of factors significantly slowed, but did not halt, developments in somatic hybridization research from the 1960s; the technique should therefore be considered a dormant biotechnology. Reconstructing the history of somatic hybridization, dominated by plant physiologists.

KEY WORDS: cell fusion, Edward C. Cocking, plant breeding, plant biotechnology, protoplasts, somatic hybrids, technological failure

If you travelled back to the 1960s to ask a respectable biologist about the most promising means of modifying crop plants, they may well have pointed you toward somatic hybridization. If you had asked the same question in the 1990s, the firm answer would be genetic modification (GM) through recombinant DNA technology. At the 1970 meeting of the British Society for Social

\*University of Leeds, Centre for History and Philosophy of Science, School of Philosophy, Religion and History of Science, Woodhouse Lane, Leeds, LS2 9JT. holmes.matthew99@ gmail.com

Abbreviations: BSSRS, British Society for Social Responsibility in Science; GM, genetic modification.

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Responsibility in Science (BSSRS) in London, Yale's Professor of Biology Arthur W. Galston exemplified the perceived importance of somatic hybridization. Speaking to a mixed audience of scientists, historians, technicians, and social radicals, Galston announced that "[o]ne can dream of many exciting possibilities" when considering a future dominated by "new somatic genetics of higher plants."<sup>1</sup> Yet in only a matter of years, this exciting future had ebbed away, to be replaced by modern biotechnology as we know it. Recombinant DNA is now synonymous with plant biotechnology.

Somatic hybridization—the fusion, resurrection, and reproduction of plant cells stripped of their cell walls (termed "protoplasts")—is a largely forgotten biotechnology.<sup>2</sup> Instead the history of modern agricultural biotechnology is dominated by the meteoric rise of molecular biology and the development of recombinant DNA technology in the United States. As such, recombinant DNA technology comes complete with its own scientific narrative. Significant names and dates include the discovery of the structure of DNA by Watson and Crick in 1953, the creation of recombinant DNA molecules in 1972, closely followed by bacterium in 1973, and so on.<sup>3</sup> Yet even during the 1970s, a recombinant DNA future was by no means a foregone conclusion. Somatic hybridization offered an alternate route to revolutionize agriculture through biotechnology. Moreover, the technology developed in a very different context. Critical developments occurred in an international academic setting, largely due to the work of plant physiologists and pathologists. By contrast,

I. Arthur W. Galston, "Molecular Biology and Agricultural Botany," in *The Social Impact of Modern Biology*, ed. Watson Fuller (London: Routledge and K. Paul, 1971), 14. The meeting provides a useful "case-study of sea-change arguments." The conference was large and represented a plethora of views and attitudes to modern science. Jon Agar, "What Happened in the Sixties?" *British Journal for the History of Science* 41, no. 4 (2008): 567–600, on 571–73.

2. Like GMOs, somatically hybridized plants keep the additional genetic information gained via fusion across the generations (although sterility poses a major barrier). Short references to somatic hybridization occur in Jack Ralph Kloppenburg Jr., *First the Seed: The Political Economy of Plant Biotechnology, 1492–2000* (Cambridge: Cambridge University Press, 1988), 192; Charles Daniel, *Lords of the Harvest: Biotech, Big Money, and the Future of Food* (Cambridge: Perseus Publications, 2001), 9; Paul F. Lurquin, *The Green Phoenix: A History of Genetically Modified Plants* (New York: Columbia University Press, 2001), 102; Rachel A. Schurman, "Introduction: Biotechnology in the New Millennium," in *Engineering Trouble: Biotechnology and Its Discontents*, ed. Rachel A. Schurman and Dennis Doyle Takahashi Kelso (Berkeley: University of California Press, 2003): 1–23, on 20. Yet somatic hybridization has yet to be subjected to thorough historical treatment.

3. Susan Wright, "Recombinant DNA Technology and its Social Transformation, 1972–1982," *Osiris* 2 (1986): 303–60, on 303.

standard histories of the development of recombinant DNA technology take place in a commercialized and localized context.  $^4\,$ 

Yet new histories have challenged the narrow, recombinant-DNA-focused narrative. The twentieth century has seen a plethora of tools and techniques harnessed to manipulate life on the cellular level. In the realm of plant breeding, these have included the use of radiation and chemicals such as colchicine to manipulate chromosomes, albeit with limited success.<sup>5</sup> The communities involved with, or supportive of, these activities were diverse. They included everyone from noted biologists to amateur plant breeders and gardeners.<sup>6</sup> Yet another community was posed to intervene in the manipulation of life. For much of the twentieth century, plant physiologists had considered their discipline best able to "study and explain biological functions and processes." By the 1960s, at the height of "Cold War technological optimism," plant physiologists had claimed not only to have achieved their goal of unlocking the underlying laws of plant physiology, but also to have overcome the barrier posed by the plant cell wall.<sup>7</sup> The removal of the cell wall promised not only the ability to study plant cells with newfound clarity, but also to merge these cells through somatic hybridization and bypass the limits of traditional sexual reproduction.

4. Martin Kenney, *Biotechnology: The University–Industrial Complex* (New Haven; London: Yale University Press, 1986); Sally Smith Hughes, "Making Dollars Out of DNA: The First Major Patent in Biotechnology and the Commercialization of Molecular Biology, 1974–1980," *Isis* 92, no. 3 (2001): 541–75; Daniel Lee Kleinman, *Impure Cultures: University Biology and the World of Commerce* (Madison: University of Wisconsin Press, 2003); Nicolas Rasmussen, *Gene Jockeys: Life Science and the Making of the First Biotech Drugs* (Baltimore: John Hopkins University Press, 2014).

5. On the use of mutation breeding in the United States, see Helen Anne Curry, *Evolution Made to Order: Plant Breeding and Technological Development in Twentieth-Century America* (Chicago and London: University of Chicago Press, 2016). On its use in Germany, see Karin Zachmann, "Peaceful atoms in agriculture and food: How the politics of the Cold War shaped agricultural research using isotopes and radiation in post war divided Germany," *Dynamis* 35, no. 2 (2015): 389–408.

6. On the latter, see Paige Johnson, "Safeguarding the Atom: The Nuclear Enthusiasm of Muriel Howorth," *British Journal for the History of Science* 45, no. 4 (2012): 551–71; Helen Anne Curry, "From Garden Biotech to Garage Biotech: Amateur Experimental Biology in Historical Perspective," *British Journal for the History of Science* 47, no. 3 (2014): 539–65.

7. David P.D. Munns, "The Phytotronist and the Phenotype: Plant Physiology, Big Science, and a Cold War Biology of the Whole Plant," *Studies in History and Philosophy of Biological and Biomedical Sciences* 50 (2015): 29–40, on 29. On the contribution of plant physiologists to molecular biology, see Doris T. Zallen, "Redrawing the Boundaries of Molecular Biology: The Case of Photosynthesis," *Journal of the History of Biology* 26, no. 1 (1993): 65–87.

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Resurrecting a little-known history that differs markedly from current conceptions of plant biotechnology contributes to a wider history of attempts to exploit the plasticity of living things. In this paper I therefore set out to reconstruct the story of somatic hybridization: its origins, key developments, heyday, and eventual decline. I begin with a brief history of early protoplast research and the background to its emergence as a possible tool for plant breeders from the 1960s, including prior work on animal cell fusion in biological and medical circles and the rise of plant physiology. Moving into the mid-twentieth century, I then relate how plant cells were first stripped of their cell walls using enzymes at the University of Nottingham's Department of Botany, which allowed a renewed interest in somatic hybridization to flourish. I next cover the heyday of somatic hybridization, including the creation of the world's first somatic hybrid (in the modern sense). Finally, I attempt to explain the failure-relative to recombinant DNA technology-of somatic hybridization as a commercial biotechnology. Cultivars of somatic hybrids did not appear until the 1990s. This late arrival was largely a consequence of technical difficulties and supply problems, which hampered research.

#### PLANT PHYSIOLOGY AND CELL FUSION

Botanists claimed to have created somatic hybrids since (at least) the early decades of the twentieth century. Yet by the 1950s botanists insisted that somatic hybrids were an impossible fable.<sup>8</sup> This inconsistency arose from long-standing arguments surrounding an age-old botanical technique: grafting. For decades, botanical textbooks claimed that plant grafts interacted at the cellular level, making them true somatic hybrids.<sup>9</sup> Yet this claim was largely abandoned, and graft hybrids were labelled as "chimeras" by 1949.<sup>10</sup> The 1965 *Encyclopaedia* 

8. F. Constabel, "Somatic Hybridization in Higher Plants," *In Vitro* 12, no. 11 (1976): 743–48, on 743.

9. Continuity between the cells of scion and stock was apparently established by some form of "protoplasmic communion," or cell fusion. W. Neilson Jones, *Plant Chimaeras and Graft Hybrids* (London: Methuen & Co., 1934), 3. Recent research suggests that some form of genetic exchange does occur across grafts. See Ignacia Fuentes et al., "Horizontal Genome Transfer as an Asexual Path to the Formation of New Species," *Nature* 511, no. 7508 (2014): 232–35. A summary is provided in Michael Le Page, "Farmers may have been accidentally making GMOs for millenia," *New Scientist* 229, no. 3064 (2016): 14, https://www.newscientist.com/article/2079813-farmers-may-have-been-accidentally-making-gmos-for-millennia/ (accessed 5 Dec 2017).

10. Constabel, "Somatic Hybridization" (ref. 8), 743.

*of Plant Physiology* was unequivocal in its dismissal of grafts as somatic hybrids. Contributor Professor F. Brabec announced that "somatic hybrids do not exist and taking all possibilities into consideration, it appears unlikely they will ever exist."<sup>11</sup> Somatic hybridization—the fusion of plant cell nuclei—faced a major natural obstacle: the seeming impenetrability of the cell wall. To create fused plant cells, it is necessary to remove their walls without damaging the contents. Plant cells devoid of their walls are now termed "protoplasts."

The first protoplasts were created in the late nineteenth century. Yet early milestones in what we now recognize as protoplast research were disconnected from more modern developments. These milestones were only recognized as significant following reviews of the scientific literature from somatic hybridization enthusiasts during the 1960s and 1970s. It was such reviews that uncovered the work of John Klercker (1866–1929), associate Professor of Botany at the University of Stockholm, who in 1892 had mechanically cut away the wall of plant cells to release their cytoplasm and observe its contents.<sup>12</sup> Protoplast fusion was subsequently observed in epidermis cells by German botanist Ernst Küster in 1910, and interspecific fusions were recorded by Küster's protégé, W. Michel, in 1937.<sup>13</sup>

Yet mechanical methods of removing the cell wall were extremely difficult and labor-intensive, limiting the number of protoplasts available for study. Writing in 1931, Janet Q. Plowe of the University of Pennsylvania's Department of Botany described the agonizing process of separating dehydrated epidermal cells of Bermuda onions from their walls, using nothing more than a blunt needle and a scalpel.<sup>14</sup> It is worth reiterating at this stage that the early

11. Brabec's section of the 1965 *Encyclopaedia of Plant Physiology* did not appear with an English translation. Constabel, "Somatic Hybridization" (ref. 8), 743.

12. Edward C. Cocking, "Plant Protoplasts," in *Viewpoints in Biology*, Vol. 4, ed. J. D. Carthy and C. L. Duddington (1965), 170–203. For the original paper, see John Klercker, "A Method for the Isolation of Living Protoplasts," *Plant Physiological Releases* 3 (1892): 463–74. Klercker's short piece can be accessed at the Digitale Sammlungen, http://sammlungen.ub.uni-frankfurt.de/ botanik/periodical/pageview/4449862 (accessed 5 Dec 2017).

13. Protoplasts can occur naturally, allowing fusion between plant cells to occur. Küster observed "naked vacuolar membranes" in the sap of solanaceous berries. Ernst Küster, "Über die Gewinnung Nackter Protoplasten," *Protoplasma* 3, no. 1 (1927): 223–34. Decades later, protoplasts, protoplasmic units, and vacuoles were observed in tomato fruit locale tissue. Edward C. Cocking and D. W. Gregory, "Organized Protoplasmic Units of the Plant Cell. 1. Their Occurrence, Origin and Structure," *Journal of Experimental Biology* 14, no. 3 (1963): 504–11.

14. Janet Q. Plowe, "Membranes in the Plant Cell. I. Morphological Membranes at Protoplasmic Surfaces," *Protoplasma* 12, no. 1 (1931): 196–220, on 197–98. Plowe saw herself within a tradition of cell research and "micromanipulation," beginning with the De Vries's 1885 study of pioneers of protoplast creation and fusion were not interested in creating somatic hybrids.<sup>15</sup> They were plant physiologists based within university botany departments. As Plowe's paper, which explained how "the existence and function of the plasma membrane" concerned physiologists "from both a practical and . . . theoretical point of view," demonstrates, their interests were focused squarely upon the plant cell, its structure and function.<sup>16</sup>

Throughout the twentieth century, plant physiologists had insisted on the primacy of their discipline within botany. By the 1950s this "self-image" manifested with a focus on the basic processes underpinning life, an experimental methodology, and a belief that plant physiology was the "leading edge of plant science."<sup>17</sup> Yet despite a sense of primacy and an experimental drive, by the 1960s protoplasts existed only as a research tool for plant physiology. However, cell fusion was of great interest to other biologists interested in fundamental questions of heredity and the plasticity of life. During the 1950s new discoveries indicated that somatic cells could exchange genetic information, leading molecular biologist and bacteriologist Joshua Lederberg (1925–2008) to criticize biologists for their "antisexual bias."<sup>18</sup> Cell fusion—and later, plant somatic hybridization—would become part of a larger project in the life sciences, aimed at testing the limits of life's plasticity.

Fusion of human and animal somatic cells had been achieved by the mid-1960s, leaving researchers surprised by the cellular compatibility, or "internal homology" of organisms.<sup>19</sup> To journalists, the fusion of human and mouse cells by Henry Harris and John Watkins in 1965 heralded everything from the creation of monsters to a new understanding of life.<sup>20</sup> Yet fusion of microbial

the tonoplast (the layer of cytoplasm around the plant vacuole). Plowe favored the term "micromanipulation" over "microdissection" for her work, as the latter implied the study of dead organisms.

<sup>15.</sup> It was only later that improvement in plant tissue culture technology made the resurrection of altered cells to full-grown plants viable. See L. G. Nickell and J. G. Torrey, "Crop Improvement through Plant Cell and Tissue Culture', *Science* 166, no. 3908 (1969): 1068–70, on 1068.

<sup>16.</sup> Plowe, "Membranes in the Plant Cell" (ref. 14), 196.

<sup>17.</sup> Munns, "The Phytotronist and the Phenotype" (ref. 7), 32.

<sup>18.</sup> Hannah Landecker, *Culturing Life: How Cells Became Technologies* (Cambridge: Harvard University Press, 2007), on 188. The source cited here by Landecker is Joshua Lederberg, "Genetic Approaches to Somatic Cell Variation: Summary Comment," *Journal of Cellular and Comparative Physiology* 52 (1958): 383–401, on 384.

<sup>19.</sup> Landecker, *Culturing Life* (ref. 18), 199. A similar trend can be seen with recombinant DNA technology, which was first applied to bacterial and animal cells before its use in plants.

<sup>20.</sup> On cell fusion and the media, see Henry Harris, *The Balance of Improbabilities: A Scientific Life* (Oxford: Oxford University Press, 1987), on 192–94; Duncan Wilson, *Tissue Culture in Science* 

and animal cells also served as a source of dialogue and inspiration for those involved in somatic hybridization. For instance, both parties were wholly reliant upon tissue culture for their work, with techniques being readily shared across disciplinary boundaries throughout the twentieth century.<sup>21</sup> As somatic hybridization developed through the 1960s and 1970s, new innovations were passed on to colleagues concerned with animal cell fusion. For instance, Henry Harris recalled how a highly effective chemical used to encourage plant cell fusion in the mid-1970s was also found to be of equal benefit for fusing animal cells.<sup>22</sup>

The twentieth century had seen a growing confidence among plant physiologists that their experimentally orientated discipline could unlock the fundamental processes of life. Part of this ambition manifested in attempts to remove the plant cell wall and study protoplasts, as attempted by Klercker and Plowe. Yet to some extent, this history of protoplast creation was an invented tradition. In 1967, controversy erupted when Swiss botanist A. Frey-Wyssling suggested that plant protoplasts should be termed "gymnoplasts." Frey-Wyssling based his challenge upon historical precedence, citing Küster's (1935) use of gymnoplasts.<sup>23</sup> Unfortunately for Frey-Wyssling, his claim to historical precedence using Küster was overridden by the (re)discovery of Klercker's 1892 manuscript.<sup>24</sup> Disputes over terminology can be seen as part of a more important struggle to construct a scientific tradition. As protoplast research dramatically surged forward during the 1960s, the creation of commercially important somatic hybrids became a tangible possibility. The recognition of who came first suddenly became a matter of urgency.<sup>25</sup>

A growing sense of purpose among plant physiologists was joined by the general realization that somatic cells could be involved in heredity. Through the

24. E. Pojnar and Edward C. Cocking, "Formation of Cell Aggregates by Regenerating Isolated Tomato Fruit Protoplasts," *Nature* 218, no. 289 (1968): 289.

*and Society: The Public Life of a Biological Technique in Twentieth Century Britain* (Basingstoke: Palgrave Macmillan, 2011), on 75.

<sup>21.</sup> Hannah Landecker, "It Is What It Eats: Chemically Defined Media and the History of Surrounds," *Studies in the History and Philosophy of Biological and Biomedical Sciences* 57 (2006): 148–60, on 153.

<sup>22.</sup> Henry Harris, *The Cells of the Body: A History of Somatic Cell Genetics* (New York: Cold Spring Harbor Laboratory Press, 1995), 142.

<sup>23.</sup> A. Frey-Wyssling, "Gymnoplasts instead of 'protoplasts'," Nature 216, no. 516 (1967): 516.

<sup>25.</sup> Just as molecular biology possesses a scientific narrative, so plant physiologists attempt to build their own, following successful advances in protoplast creation. Whereas the former finds its origins in the 1953 discovery of DNA, Cocking found his in Klercker's release of the protoplast in 1892.

1950s and 1960s, biological researchers were astonished to find that very different organisms were compatible on the cellular level: somatic hybridization would therefore operate alongside a wider scientific discourse on the possibilities offered by cell fusion. By the 1960s, therefore, the stage was set for the revival and future development of protoplast research with a new aim: the creation and reproduction of somatic hybrids. Research into protoplasts and somatic hybridization would initially take place within the world of plant physiology, rather than the realm of molecular biology. All that stood in the physiologist's way was the barrier posed by the cell wall: a barrier that would be eventually be overcome using an enzymatic method recommended by microbiologists.

## **PROTOPLAST PRODUCTION**

A key moment in the modern history of somatic hybridization occurred at the University of Nottingham's Botany Department in 1960. Some forty years later, its principal instigator and lecturer in plant physiology, Edward C. Cocking, recounted the event. Cocking was attempting to develop a new cell culture method. Noting that cell division did not occur in tomato root cells, he speculated that releasing the cell contents from their confining wall would aid the culture process. Drawing upon discussions with workers at the Microbiological Research Establishment in Porton, Cocking decided that the use of a cellulase enzyme would be most effective for degrading plant cell walls.<sup>26</sup> Fruitless attempt after fruitless attempt followed. Commercially available enzyme preparations were simply not up to the task. A promising avenue finally opened when Cocking came across the studies of D. R. Whitaker of the National Research Laboratories in Ottawa, who had developed his own cellulase preparation. When Cocking tested Whitaker's preparation, the solution was a complete success, releasing protoplasts.<sup>27</sup>

What was the significance of applying Whitaker's enzyme preparation to plant cells? Cocking's initial report to *Nature* (1960) on the phenomenon was purely descriptive. Yet a paper published the following year showed developments in both his techniques and ideas on the use of protoplasts. Cocking noted that "liberated bacterial and fungal protoplasts" were of great value in

<sup>26.</sup> Edward C. Cocking, "Plant protoplasts," *In Vitro Cellular & Developmental Biology* 36, no. 2 (2000): 77–82, on 77.

<sup>27.</sup> Edward C. Cocking, "A Method for the Isolation of Plant Protoplasts and Vacuoles," *Nature* 187, (Sep 1960): 962–63.

"morphological, biochemical and genetic work."<sup>28</sup> Protoplasts released from the root tips of tomato seedlings in Cocking's laboratory "indicated their unique potentiality for similar studies."<sup>29</sup> More important was an unspoken truth. An enzymatic means of creating protoplasts freed physiologists from the constraints of micromanipulating cells via surgical instruments, as described by Plowe in 1931. Relatively speaking, protoplasts could now be created quickly and in the large numbers required for research. Yet in these early years, experiments conducted at the University of Nottingham focused solely upon means of harnessing protoplasts to solve "present problems associated with growth and differentiation in plants."<sup>30</sup> Somatic hybridization had yet to re-enter the scientific discourse.

Scientists at the University of Nottingham may have been reticent to make wild claims regarding the potential of protoplasts for plant breeding. Yet other biologists were not so reserved, excitedly noting the potential for somatic hybridization. Speaking at the 1970 BSSRS meeting, Arthur Galston embodied this excitement. But why did naked cells in a Nottingham laboratory so excite this Professor of Biology? In the spirit of a conference sceptical of scientific triumphalism, Galston characterized intensive agriculture as beset by technological problems, from overreliance on fertilizers to disease-vulnerable monocultures.<sup>31</sup> Radical advances in plant breeding would be required to produce new plants capable of yielding more food at a lower cost to the environment. This issue was made all the more pressing by the publication of Rachel Carson's *Silent Spring* (1962), which revealed the extent of environmental damage caused by indiscriminate pesticide use in industrialized agriculture.

Only a year before the BSSRS conference, Paul Ehrlich (1968) published his own bestselling work *The Population Bomb*. The book warned of the precise dangers to modern agriculture cited by Galston, including the environmental degradation caused by nitrogen fertilizers, while predicting global food shortages from overpopulation. Population concerns would be featured in a prominent fashion at the first Earth Day in 1970.<sup>32</sup> On the one hand,

28. Edward C. Cocking, "Properties of Isolated Plant Protoplasts," *Nature* 191, no. 4790 (1961): 780–82, on 780.

32. Ibid., 158. Thomas Robertson, *The Malthusian Moment: Global Population Growth and the Birth of American Environmentalism* (New Brunswick, NJ: Rutgers University Press, 2012), 168–71. Ehrlich's work formed part of a wider neo-Malthusian literature, which emerged in the post-war

<sup>29.</sup> Ibid., 780.

<sup>30.</sup> Ibid., 781.

<sup>31.</sup> Galston, "Molecular Biology" (ref. 1), 158.

industrialized agriculture was a source of pollution and environmental damage. Yet growing more food was one way to counter the looming population crisis. Among a number of promising solutions discussed by Galston was somatic hybridization. Referring to Cocking's removal of the plant cell wall, Galston announced that somatic hybrids might one day emerge, possessing remarkable qualities—from nitrogen fixing to disease resistance.<sup>33</sup>

Within purely scientific exchanges, a similar level of excitement was displayed. At a 1969 meeting of plant physiologists and geneticists, somatic hybridization was designated by observers to be "still experimental, but . . . show[ing] great promise."<sup>34</sup> Suggestions arose that sexual barriers to the crossing method in plant breeding could be overcome. Advances in protoplast manipulation hinted that "asexual fusion might become a major method for 'crossing' unrelated plants which are not easily crossed using sexual methods."<sup>35</sup> Reported in *Science*, the meeting "Crop Improvement through Plant Cell and Tissue Culture" was no minor affair and included important figures such as Cocking.<sup>36</sup> Yet despite the sanguinity of the attendees and Galston's optimism, it had now been some ten years since Cocking first harnessed enzymes to release protoplasts. Not one plant had yet been created using somatic hybridization.

Two barriers stood in the way of somatic hybrids. Once released from the confines of their cell wall, protoplasts were no longer viable as living cells outside of their nurturing medium. Vulnerable to the environment, the regeneration of a new cell wall was necessary for their long-term survival. With this achieved, efforts could then turn to growing viable plants from protoplasts. These barriers were overcome by the efforts of Japanese researchers. In 1970, Toshiyuki Nagata and Itaru Takebe of the Institute for Plant Virus Research in Chiba, Japan, observed protoplasts regenerating their lost walls. Their subject, tobacco mesophyll, was also capable of cell division.<sup>37</sup> Takebe was hopeful. Citing then-unpublished observations, he stated his belief that protoplasts

era. For an overview, see Mauricio Schoijet, "Limits to Growth and the Rise of Catastrophism," *Environmental History* 4, no. 4 (1999): 515–30.

<sup>33.</sup> Galston, "Molecular Biology" (ref. 1), 159. Disease resistance in plant varieties was a major concern, as monoculture led to a narrow genetic base in key crops: a weakness highlighted by a 1970 outbreak of southern corn leaf blight, which destroyed fifteen percent of the corn crop in the United States. Kloppenburg, *First the Seed* (ref. 2), 122.

<sup>34.</sup> Nickell and Torrey, "Crop Improvement" (ref. 15), 1068.

<sup>35.</sup> Ibid., 1068.

<sup>36.</sup> Ibid., 1070.

<sup>37.</sup> Toshiyuki Nagata and Itaru Takebe, "Cell Wall Regeneration and Cell Division in Isolated Tobacco Mesophyll Protoplasts," *Planta* 92, no. 4 (1970): 301–08, on 303–04.

were capable of fusion, offering "a unique experimental material for plant genetics."<sup>38</sup> Collaboration between Takebe and researchers at the Max Planck Institut für Biologie in Tübingen the following year saw the regeneration of a whole plant from protoplasts. These results established "for the first time that cell protoplasts from the mesophyll can be cultured to give rise to whole plants."<sup>39</sup> Extensive cell division in protoplasts opened new possibilities, including "the breeding of new plants through somatic hybridization."<sup>40</sup>

Given the pre-existing interest of plant physiologists in protoplast work, it comes as little surprise that an enzymatic means of releasing protoplasts was first developed in a botany department. Cocking's work raised much interest, with funding for future research provided by esteemed bodies such as the Royal Society and the Department of Scientific and Industrial Research.<sup>41</sup> The regeneration of whole plants from protoplasts marked another important step toward a new future in plant breeding, one dominated by somatic genetics. These results also emerged from the plant sciences sector, albeit a plant pathology institute, rather than a department of botany. The shift in protoplast research to Japan is explained by that country's advanced, enzyme production facilities.<sup>42</sup> The cellulase enzyme used for protoplast production was produced commercially in Japan from 1968, allowing domestic researchers easy access to the raw ingredients necessary for advanced work with plant protoplasts. Although Takebe, Labib, and Melchers had openly invoked the possibility of somatic hybrids in 1971, the actual regeneration of a higher plant from fused protoplasts would take place the following year in the United States.

#### THE GLORY PERIOD

In 1972—a year usually associated with the first recombinant DNA molecules—a team at the Department of Biology at Brookhaven National Laboratory used protoplast fusion to create an interspecific plant hybrid.<sup>43</sup>

40. Ibid., 320.

- 41. Cocking, "Properties of Isolated Plant Protoplasts" (ref. 28), 782.
- 42. Cocking, "Plant protoplasts" (ref. 26), 78.

43. David A. Jackson et al., "Biochemical Method for Inserting New Genetic Information into DNA of Simian Virus 40: Circular SV40 DNA Containing Lambda Phage Genes and the

<sup>38.</sup> Ibid., 307.

<sup>39.</sup> I. G. Takebe et al., "Regeneration of Whole Plants from Isolated Mesophyll Protoplasts of Tobacco," *Naturwissenschaften* 58 (1971): 318–20, on 320.

This achievement marked a major advance in the field of somatic hybridization, moving the fledgling technology one step closer its ultimate commercial aim: creating new varieties of enhanced crop plants in agriculture. Human manipulation had essentially overcome the usual sexual barriers to species crosses. The Brookhaven team's paper, published in the *Proceedings of the National Academy of Sciences*, bore clear references to the difficult and terminologically confusing past of somatic hybridization. Nagata and Takebe's experimental conditions and regeneration medium were also exactly recreated.<sup>44</sup> The Brookhaven team also sought to distance their hybrid protoplasts from grafting. Their paper described how tumor formation on the stem of their tobacco plant did not occur following a "graft union," instead being characteristic of a first-generation (F<sub>1</sub>) hybrid and amphiploid.<sup>45</sup>

Brookhaven's hybrid tobacco plant can be safely said to mark the beginning of somatic hybridization. By 1977, Cocking and his colleagues had developed their laboratory methods to create somatic hybrids from sexually incompatible species.<sup>46</sup> Kloppenburg has described how a period of "bio-hype" surrounded genetic engineering during the 1970s, before giving way to a "traditional concern" with practical products.<sup>47</sup> The hype surrounding somatic hybridization encompassed both decades, largely occurring in Britain and the United States. Although the technique was recognized as an important "breakthrough in cytological and genetical methodology," supporters seized upon its potential to bypass "the limits of traditional plant breeding."<sup>48</sup> Somatic hybridization was not only recognized within scientific circles. Addressing the Economic Club of Detroit in 1980, Clifton R. Wharton Jr., Chancellor of the State

Galactose Operon of *Escherichia coli*," *Proceedings of the National Academy of Sciences* 69, no. 10 (1972): 2904–09. As early as 1948, the Brookhaven Department of Biology had hired geneticist and plant breeder W. Ralph Singleton, and was involved in testing the effects of radiation on crop plants. See Curry, *Evolution Made to Order* (ref. 5), 147.

<sup>44.</sup> Peter S. Carlson et al., "Parasexual Interspecific Plant Hybridization," *Proceedings of the National Academy of Sciences* 69, no. 8 (1972): 2292–94, on 2292.

<sup>45.</sup> Ibid., 2293.

<sup>46.</sup> Edward C. Cocking et al., "Selection Procedures for the Production of Inter-Species Somatic Hybrids of *Petunia hybrida* and *Petunia parodii*. II. Albino Complementation Selection," *Plant Science Letters* 10, no. 1 (1977): 7–12.

<sup>47.</sup> Kloppenburg, *First the Seed* (ref. 2), 200. Hype can lead biotechnology through phases of "legitimation" and "delegitimation," a shift apparent in the history of somatic hybridization. Nik Brown, "Hope against Hype—Accountability in Biopasts, Presents and Futures," *Science Studies* 16 (2003): 3–21, on II–I2.

<sup>48.</sup> Constabel, "Somatic Hybridization" (ref. 8), 747.

University of New York, included somatic hybridization alongside germplasm banks as a future means of combating world hunger.<sup>49</sup>

In 1981, an issue of the Philosophical Transactions of the Royal Society entitled "The Manipulation of Genetic Systems in Plant Breeding" was published, which included a number of articles on somatic hybridization. The issue was not only significant for advocates of somatic hybridization, but also discussed numerous breeding techniques and challenges facing contemporary plant scientists and breeders. Cocking noted a marked improvement in the commercial prospects of somatic hybridization, several horticultural and crop species having been created through protoplast fusion.<sup>50</sup> Yet he also acknowledged that further research and close collaboration with breeders would need to occur before protoplasts (whether through cloning at the cellular level or somatic hybridization) would "add significantly to the armoury of the plant breeder."<sup>51</sup> Geneticist Sir Kenneth Mather was more upbeat, asserting that the main obstacle to the development of new crop varieties through somatic hybridization was the regeneration of whole plants from protoplasts. Recent advances in regeneration and tissue culture made this obstacle less daunting, leading Mather to claim that regeneration from protoplasts would "soon be achieved in our cereals."<sup>52</sup>

As the 1980s progressed, somatic hybridization continued to appear in scientific publications on plant breeding and biotechnology, albeit accompanied by a promising newcomer: genetic manipulation through recombinant DNA. The latter become a viable agricultural technology in 1983, with the first permanent uptake of genetic information by a plant.<sup>53</sup> Simultaneous achievements occurred in the production of somatic hybrids, including a (infertile) cross between a potato and tomato.<sup>54</sup> In 1985, M. W. Fowler of the Wolfson

49. Wharton was a member of the Presidential Commission on World Hunger, which delivered its final report to President Carter in March 1980. Clifton R. Wharton Jr., "Food, the Hidden Crisis," *Science* 208, no. 4451 (1980): 1415.

50. Edward C. Cocking, "Opportunities from the Use of Protoplasts," *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences* 292, no. 1062 (1981): 557–68, on 557.

51. Ibid., 566.

52. Kenneth Mather, "Perspective and Prospect," *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences* 292, no. 1062 (1981): 601–29, on 607. In reference to W. Wernicke and R. Brettell, "Somatic Embryogenesis from Sorghum Bicolour Leaves," *Nature* 287 (Sep 1980): 138–39.

53. M. V. Bevan et al., "A Chimeric Antibiotic Resistance Gene as a Selectable Marker for Plant Cell Transformation," *Nature* 304 (1983): 184–87.

54. J. F. Shepard et al., "Genetic Transfer in Plants through Interspecific Protoplast Fusion," *Science* 219, no. 4585 (1983): 683–88.



**FIG. 1.** A regenerated cluster of cells, or callus, grown from protoplasts. Image from Tina Lorraine Barsby, "Towards Somatic Hybridisation in the Genus *Solanum*" (PhD dissertation, University of Nottingham, 1981).

Institute of Biotechnology in Sheffield listed the techniques protoplast fusion and genetic manipulation side-by-side in a review of methods in cell and tissue culture.<sup>55</sup> Yet for Fowler, somatic hybridization remained a potential tool in agriculture, rather than a practical reality.<sup>56</sup>

In 1984, an international symposium on genetic manipulation in crops was held in Beijing. Li Xianghui of the Academia Sinica's Institute of Genetics used his platform to note that somatic hybridization had been hampered by resulting hybrid plants failing to display even a "minimal level of fertility."<sup>57</sup> Technical difficulties hampered somatic hybridization, at the very moment that recombinant DNA technology began to display agricultural applications. Yet all was not lost. At the same symposium, a team comprising

55. M. V. Fowler, "Plant Cell Biotechnology and Agriculture: Impacts and Perspectives," *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences* 310, no. 1144 (1985): 215–20, on 215.

56. Ibid., 220.

57. Li Xianghui, "Advances in Plant Genetic Manipulation," in *Genetic Manipulation in Crops*. Natural Resources and the Environment Series, Vol. 22, Proceedings of the International Symposium (Beijing, Oct 1984). (London: Cassell, 1988), 219–20.



**FIG. 2.** The formation of shoots, roots, flowers and fruits from a callus. Image from Tina Lorraine Barsby, "Towards Somatic Hybridisation in the Genus *Solanum*" (PhD dissertation, University of Nottingham, 1981).

members of Agriculture Canada and Carleton University's Biology Department announced practical advances in cultivar creation through somatic hybridization. Working on a tobacco breeding program, researchers had somatically crossed two varieties, selected for their disease resistance and elevated nicotine levels.<sup>58</sup> Unlike their predecessors, these hybrids displayed useable levels of fertility. Some twenty somatic hybrid lines were transferred from Ottawa to Delhi, to be incorporated into a backcrossing program.<sup>59</sup> This line of research finally paid dividends. Some ten years after the

58. W. A. Keller, R. S. Pandeya, S. C. Gleddie, and G. Setterfield, "Application of Somatic Hybridization Technology to Plant Breeding," in *Genetic Manipulation in Crops*. Natural Resources and the Environment Series, Vol. 22, Proceedings of the International Symposium (Beijing, Oct 1984). (London: Cassell, 1988), 192.

59. Ibid., 192.

symposium, a commercial crop of tobacco created through somatic hybridization was planted in Ontario. $^{60}$ 

Closing the 1984 symposium, W. R Scowcroft of the Commonwealth Scientific and Industrial Research Organisation's division of plant industry gave his reflections. Scowcroft chose to emphasize the importance of plant biotechnology, which, under his definition, included techniques in tissue culture and genetic engineering.<sup>61</sup> He described the ability to produce large numbers of protoplasts and to induce their regeneration into plants as a "truly remarkable technological achievement."<sup>62</sup> Protoplast fusion was a different matter. Although somatic hybridization allowed "the circumnavigation of barriers to sexual hybridization," fertility problems meant it was "still uncertain whether somatic hybridization will permit useful nuclear gene introgression for crop improvement."63 As GM crops achieved success and provoked controversy on the international scene during the 1990s, news from the world of somatic hybridization was muted. Notable milestones were achieved during this time, particularly in Canada. Yet the fact remains that somatic hybridization achieved nothing like the status and ubiquity of GM in agriculture. The final section of this paper will examine the reasons for this disappointing performance in commercial farming and ask if we should consider somatic hybridization an example of technological failure.

#### THE LONG, SLOW DECLINE

The story of somatic hybridization appears to be one of unrealized ambition, despite vast potential. Why then, are fields of somatically hybridized crops absent from our countryside? The large chronological gaps present in the reconstructed story of somatic hybridization offer some indication. If recombinant DNA was a rapidly emerging technology, then protoplast fusion moved at a snail's pace. The technique was later described by British geneticist Norman

60. Norman W. Simmonds and J. Smartt, *Principles of Crop Improvement*, 2nd ed. (Oxford: Blackwell Science, 1999), 290.

61. W. R. Scowcroft, "Genetic Manipulation in Crops: A Symposium Review," in *Genetic Manipulation in Crops*. Natural Resources and the Environment Series, Vol. 22, Proceedings of the International Symposium (Beijing, Oct 1984). (London: Cassell, 1988), 13.

62. Ibid., 15.

63. Ibid., 15, described genetic manipulation as "a truly generalised method for plant genetic transformation."

Simmonds as "theoretically elegant, but technically demanding."<sup>64</sup> Yet the difficulty involved in creating and fusing protoplasts is only part of the explanation.

Results from protoplast research came periodically. It was over a decade after Cocking first used an enzymatic procedure to create protoplasts that the next step toward somatic hybrids was made: the regeneration of the cell wall of protoplasts.<sup>65</sup> Reflecting upon this gap, Cocking would later describe how his isolation of protoplasts "was ahead of the then[-]technology of plant cell-wall-degrading enzyme production."<sup>66</sup> Shortages of enzyme held back the work of plant scientists at the University of Nottingham. The personal interests of Cocking also held back protoplast work. By his own admission, Cocking was more interested in light microscopy and electron microscopy during the early 1960s, inspired by his work with Irene Manton at the University of Leeds and Heinrich Matthaei in Göttingen. Even if large amounts of commercially available enzymes were available, Cocking considered it "unlikely" that he would have become a pioneer in protoplast fusion.<sup>67</sup>

Cellulase enzyme was made commercially available in Japan in 1968, for use in baby food and biscuit manufacturing. This enabled Japanese protoplast researchers like Nagata and Takebe to carry out their experiments.<sup>68</sup> Yet enzyme shortages continued elsewhere. A 1974 letter from Keith Roberts of the John Innes Institute to James Watson (located at Cold Spring Harbor Laboratory) discussed the possibility of the Institute running a course on higher plant cell protoplasts. Despite promising steps in resurrecting somatic plant cells, Roberts identified ongoing difficulties in the field, not least a lack of published literature. The laboratory setup required for a course was relatively simple: a greenhouse, tissue culture facilities, water baths, and bench centrifuges. Yet Roberts did note that cellulase enzymes constituted a significant expense, being directly obtained from Japan.<sup>69</sup> As a cutting-edge biotechnology, protoplast production was ahead of existing enzyme production techniques, therefore requiring rare and expensive materials. The development of protoplast research (and hence somatic hybrids) was significantly slowed by enzyme shortages during the 1960s and even into the 1970s.

68. Ibid., 78.

69. Letter from Keith Roberts to James D. Watson, 1974-11-18, JDW/2/2/1550/52, James D. Watson Collection, Cold Spring Harbor Laboratory archives repository.

<sup>64.</sup> Simmonds and Smartt, Principles of Crop Improvement (ref. 60), 288.

<sup>65.</sup> Nagata and Takebe, "Cell Wall Regeneration" (ref. 37), 303-04.

<sup>66.</sup> Cocking, "Plant protoplasts" (ref. 26), 78.

<sup>67.</sup> Ibid., 78-79.

Technical difficulties with the technology became increasingly evident following the creation of the first somatically hybridized plant in 1972 at Brookhaven National Laboratory. A close reading of the 1972 Proceedings of the National Academy of Sciences paper reveals that somatic hybridization was not only extremely complex, but once again ran ahead of existing technology and practices in the biological sciences. Protoplast fusion was not a precise technique. The Brookhaven team found that about a quarter of their protoplasts were actually involved in a "fusion event" (unusually efficient for the time), and even fewer of these contained the genetic information from both parent plants necessary for regeneration.<sup>70</sup> Although an impressive achievement, the somatically hybridized tobacco created at Brookhaven was far from a commercially viable organism. Shoots and leaves developed, but not roots, leading the team to graft their new shoots onto the stems of other plants to further observe the development of their somatic hybrids. Furthermore, spontaneous tumors were observed to develop on the stems of the somatic hybrids.<sup>71</sup> The new plants were delicate and unstable. Yet an equally important and difficult challenge for the researchers was determining whether their new tobacco plants were true somatic hybrids.

Three promising isolates (regenerated plants) were selected for testing to confirm that somatic hybridization had taken place. The Brookhaven team largely relied upon detailed morphological observations, which gave circumstantial evidence that their isolates were somehow different from either parent species.<sup>72</sup> Yet morphological characteristics could only be relied upon to a certain extent. These characteristics were not necessarily representative of genetic differences and did not indicate exactly which chromosomes had been exchanged between protoplasts. On a practical level, morphology was slow work, requiring researchers to wait for plants to fully develop before required measurements could be taken.

Other means of determining whether and to what extent protoplast fusion had occurred were also used by the Brookhaven team. Electrophoretic analysis demonstrated that the new plants possessed differences in their protein makeup, yet electrophoresis did not show which chromosomes had been exchanged, and was a relatively crude tool for protein fingerprinting of plants by the early 1970s.<sup>73</sup> Extracting chromosomes from the young leaves of the

<sup>70.</sup> Carlson et al., "Parasexual Interspecific Plant Hybridization" (ref. 44), 2292.

<sup>71.</sup> Ibid., 2292–93.

<sup>72.</sup> Ibid., 2293.

<sup>73.</sup> Ibid., 2292.

growing plants gave a more definite answer. These samples contained a chromosome number of 42, not unexpected when "the complexity of the fusion event and divisions after fusion" prevented the complete exchange of chromosomes from the parental protoplasts.<sup>74</sup> It was this very unpredictability that led geneticists like Simmonds to dismiss somatic hybridization as an overly complex biotechnology. Uncertainty and genetic instability caused by the uncontrolled mixing of chromosomes was not an endearing trait of somatic hybridization.

So far, somatic hybridization has been portrayed as a research topic of international interest, crossing disciplinary boundaries between plant science and genetics with ease. Yet international collaboration was hampered by disciplinary boundaries. A 1984 book on somatic hybridization by Yury Gleba and Konstantin Sytnik, both based in the Ukrainian Academy of Sciences, noted that work on hybridizing somatic cells had been carried out almost entirely by plant physiologists, not plant geneticists. Physiologists had designed methods for cell and protoplast isolation, yet an "instillation of genetic ideology and the strict logic of genetic experiments" were needed for further progress. A lack of practical progress and subsequent benefits for plant breeders may have tempered enthusiasm for somatic hybridization. Gleba and Sytnik centered themselves within the biological revolution. Distinct from the "passive" analysis of organisms, somatic hybridization embodied the "synthetic" spirit and purpose of genetic engineering. For them, recombinant DNA technology was in no way seen as superior, as "[t]he results of the experiments [on somatic hybridization] reported on in this book force us to believe more and more that the way chosen by their authors for sculpting a novel plant is the efficient one."75

The development of recombinant DNA technology is portrayed as highly focused, in stark contrast to the geographic and disciplinary divides surrounding work on somatic hybridization. The former arose from biotech firms in the United States, the product of a merger of university biology and commerce.<sup>76</sup>

75. Yury Y. Gleba, Konstantin M. Sytnik, and Robert L. Shoeman, eds., *Protoplast Fusion: Genetic Engineering in Higher Plants* (Berlin: Springer-Verlag, 1984), 179–88. Cocking reviewed Gleba and Sytnik's monograph and described it as "essential reading." Cocking referred to the author's call for an "instillation of genetic ideology" as "unfortunate phraseology." Edward C. Cocking, "*Protoplast fusion. Genetic engineering in higher plants* by Y. Y. Gleba and K. M. Sytnik. Springer-Verlag, Berlin. 1984," *Heredity* 57, no. 3 (1986): 432.

76. Kenney, *Biotechnology* (ref. 4); Smith Hughes, "Making Dollars" (ref. 4); Kleinmann, *Impure Cultures* (ref. 4); Rasmussen, *Gene Jockeys* (ref. 4).

<sup>74.</sup> Ibid., 2293–94.

Yet commercial links alone cannot completely account for the rise of DNAbased technology. Unlike protoplast fusion, recombinant DNA technology was applicable to a wide range of activities in the biological sciences, hence its adoption by "molecular biology laboratories around the world."77 Somatic hybridization was instead the preserve of plant scientists, hence the complaints of Gleba and Sytnik. Cocking believes it was the genetic expertise of the Brookhaven team that allowed them to create the first somatic hybrid; in fact, geneticists initially turned to protoplasts in their quest to modify organisms.<sup>78</sup> Yet a number of factors ultimately favored the uptake of recombinant DNA technology as the go-to method of genetic modification of plants. It was not simply a matter of recombinant DNA being a far easier or more reliable technology, as the creation of GM plants still involves elements of chance and wastefulness. Recombinant DNA was also favored by its place within the rising discipline of molecular biology, leading to widespread interest from both science and industry. Yet this is not to say that somatic hybridization research suffered from a lack of investment. Cocking, for instance, found himself with sixteen years' worth of funding from the United Kingdom's Agricultural Research Council in 1969.79

Can somatic hybridization be classed as a failed technology? If so, why is it worth examining? The criteria for classifying an innovation as failed can include marketing performance, efficiency of development, favorable management characteristics, effective communication, and understanding of user needs.<sup>80</sup> Under many of these criteria, somatic hybridization can be classed as a failed technology for approximately twenty years, encompassing the 1970s and '80s. In this time, somatic hybridization did not create commercial plant breeds, and the technique was plagued by slow and sporadic development. Its complexity and unpredictable nature was also uninviting to users: namely, plant breeders. Cocking was aware of this problem, urging "protoplast workers" to engage in "a continuing dialogue with breeders."<sup>81</sup> Yet there are recognized benefits to studying a seemingly failed innovation.

In a study of the General Electric Research Laboratory, Helen Anne Curry describes a failed research program that struggled to use x-rays to induce

<sup>77.</sup> Smith Hughes, "Making Dollars" (ref. 4), 542.

<sup>78.</sup> Cocking, conversation with author, 24 Mar 2016.

<sup>79.</sup> Cocking, "Plant protoplasts" (ref. 26), 80.

<sup>80.</sup> Hans-Joachim Braun, "Introduction [to symposium on "failed innovation"]," *Social Studies of Science* 22, no. 2 (1992): 213–30, on 216.

<sup>81.</sup> Cocking, "Opportunities from Protoplasts" (ref. 50), 566.

beneficial mutations in plants during the 1920s and '30s. Ultimately, the only marketable product to emerge from the laboratory was a single variety of ornamental lily.<sup>82</sup> Yet even this relatively small case study speaks to a number of contemporary themes, including the belief in the plasticity of organisms when subject to technological intervention and collaboration between different scientific disciplines. Likewise, somatic hybridization is revelatory of both the ambitions of plant physiology and wider collaborative attempts to exploit the plasticity of living things on the cellular level from the 1960s. Somatic hybridization is yet another example of a technique that has been largely "lost to the history of biotechnology, and yet constitute[s] an important component of that history."<sup>83</sup>

## ALTERNATIVE HISTORIES OF BIOTECHNOLOGY AND THEIR VALUE

The dominance of recombinant DNA technology has extended not only to farmers' fields, but to history as well. In reconstructing an account of a little-known form of biotechnology, I have attempted to show that this dominance was not inevitable. Somatic hybridization is a technically exacting technique, but with its fair share of misfortune. At the right time, a surplus of cellulase enzyme, the support of geneticists, or mishaps in the development of recombinant DNA for agricultural use may all have shifted the balance of history in its favor. Somatic hybridization continues to be taken seriously as a plant breeding technique, even if its returns are meager. To dismiss its story would be a serious misstep, and not only on the grounds of historical nuance. Plant breeding is often a slow affair, with innovations taking years or even decades to reach their full potential. Somatic hybridization—still a relative newcomer—may yet have its day in the sun.

Even if somatic hybrids are, commercially speaking, a lost cause, their existence speaks to important points on our understanding of biotechnology on a number of levels. The first is a historiographical matter. There is an ongoing debate in historical circles over the meaning and scope of what we term "biotechnology"—a perplexity reflected in current definitions released by industry and government. This was characterized as a divide between

<sup>82.</sup> Helen Anne Curry, "Industrial Evolution: Mechanical and Biological Innovation at the General Electric Research Laboratory," *Technology and Culture* 54, no. 4 (2013): 746–81.

<sup>83.</sup> Ibid., 747.

"ancients" and "moderns" in a 1986 edition of the French biotechnology journal *Biofutur*.<sup>84</sup> A modern view of biotechnology does not begin until the discovery of the structure of DNA in 1953 and developments in molecular biology. Advocates of the ancient view embraced a much wider conception of biotechnology. A three-stage history of biotechnology is envisioned: moving from Egyptian and Babylonian brewing, to Pasteurian-informed "rational fermentation," and finally to "genetically based molecular biology."<sup>85</sup> Somatic hybridization does not fit into any of the aforementioned conceptions or categories. The technique is certainly not a form of brewing or rational fermentation, but nor does it manipulate organisms on the genetic level.<sup>86</sup>

As a method of transplanting chromosomes across the species divide, somatic hybridization seems to defy traditional categories within biotechnology. Somatic hybridization instead lends itself to a certain view of the history of plant breeding, as a series of often overlapping developments. In this view, the lines between the different forms of plant breeding are weaker and more blurry than commonly assumed. New forms of biotechnology are regularly marketed as revolutionary, with their practitioners declaring that they are the first to have attained "a properly engineered biology."<sup>87</sup> Broader histories of biotechnology lead us to question these claims, and suggest that past forms of biotechnology should not be so easily cast off.

The importance of plant physiologists, and even plant pathologists, within the history of somatic hybridization also demonstrates that biotechnology has involved a broad array of biological disciplines. Moreover, these disciplines have not operated in isolation. Dialogue between researchers blurred the boundaries among microbial, animal, and plant cell fusion, as demonstrated by Cocking's turn to the Microbiological Research Establishment for advice in 1960. Somatic hybridization is only part of a wider history of attempts to harness the internal plasticity of organisms to bypass the limitations of

84. Jean Comar, "La biotechnologie n'est plus ce qu'elle était," Biofutur 5 (1985).

85. Robert Bud, "Biotechnology in the Twentieth Century," *Social Studies of Science* 21, no. 3 (1991): 415–57, on 416–17.

86. Somatic hybridization does fit within a far more general historiographical theme: that of the molecularization of the life sciences. Yet this is problematic, as the molecularization story is generally associated with molecular biology. For a succinct synopsis of the literature, see R. Steven Turner, "Potato Agriculture, Late Blight Science, and the Molecularization of Plant Pathology," *Historical Studies in the Natural Sciences* 38, no. 2 (2008): 223–57, on 223–24.

87. Luis Campos, "That Was the Synthetic Biology That Was," in *Synthetic Biology: The Technoscience and its Societal Consequences*, ed. Markus Schmidt et al. (Heidelberg: Springer, 2009), 5–21, 16.

"traditional" breeding and crossing. This "parasexual" approach to life also led to the realization that "biological incompatibility," including the species barrier, was practically nonexistent at the cellular level.<sup>88</sup> Just as barriers against the crossing of organisms were dissolved by cell fusion, so barriers between scientific disciplines were dissolved by a shared interest in the fundamental questions of life—not least, how far life could be manipulated for the purposes of humankind.

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